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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/005,467
Filing Date: December 04, 2001
Appellant(s): ALLEN, KEITH D.

John Burke

For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 11/15/05 appealing from the Office action mailed 3/22/05.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner.

The rejection of claims 28-32, 37, 47, 52-54 and 57 under 35 U.S.C. 112 1st paragraph (new matter) is withdrawn in light of Appellant's amendment.

The rejection of claim 32 under 35 U.S.C. 112 2nd paragraph is withdrawn in light of Appellant's amendment.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Ogata et al., 1998. Journal of Biological Chemistry. Vol. 274, No. 18, pp. 12905-12909.

Sigmund, C.D., 2000. Arterioscler Thromb Vasc Biol.20:1425-1429.

Wall, R.J., 1996. Theriogenology 45:57-68.

Jacks et al., 1992. Nature, Vol 359, pp. 295-300.

Olsen 2000. GABA in the Nervous System, pp. 81-95.

Elchebly et al., 1999. Science Vol 283:1544.

http://www.mercksource.com

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 101 and 112 1st paragraph

Claims 28-32, 37, 47, 53-57 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility.

The claims are drawn to a transgenic mouse whose genome comprises a null allele in the endogenous PTP36 gene (28, 53-57). The claims are also drawn to female homozygous PTP36

knockout mouse displays one of the following phenotype: uterine dilation, keratin in the uterine horns or lumen, increased liver weight, increased spleen weight, increased thymus weight, increased liver weight relative to body weight, increased spleen weight relative to body weight (29-32). The claims are further drawn to a method of making said mouse, and cells and tissues isolated from said mouse (37).

No well-established utility exists for the claimed transgenic mouse. However, the specification asserts or implies the following as credible, specific and substantial patentable utilities for the claimed transgenic knockout mouse and cells or tissues isolated from said mouse:

1) To be used in methods of identifying agents capable of affecting a phenotype of said mouse.

2) To identify agents useful as therapeutic agents for treating conditions associated with a disruption or other mutation of the PTP36 gene.

3) To identify agents having an effect on PTP36 expression or function.

4) To test and develop new treatments relating to the behavioral phenotypes.

Each of the following shall be addressed in turn:

1) To be used in methods of identifying agents capable of affecting a phenotype of said mouse. This utility is not substantial because the specification does not disclose a utility for such agents. In other words, why would a skilled artisan wish to identify such agents? The prior art (Ogata et al., 1998, from IDS) teaches PTP36 is involved in the regulation of cell adhesion, cell growth and cytoskeleton in Hela cells. However, it is not known to be associated with any disorder that have the symptom of increased liver, spleen, thymus weight or uterine dilation, presence of keratin in the uterine horns or lumen. The disclosed phenotype of the instantly

claimed mouse, increased liver, spleen, thymus weight, or uterine abnormality (in female mice only) do not correlate with the hypothesized function of PTP36 in focal adhesion. Although the agents can affect a phenotype in said transgenic mouse or a cell/tissue isolated from said mouse, the utility is not substantial because there is no other use of said agents except affecting a phenotype that only exists in a mouse. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not credible, specific or substantial.

2) To identify agents useful as therapeutic agents for treating conditions associated with a disruption or other mutation of the PTP36 gene. This utility is not credible and specific because the specification does not disclose what kind of conditions is associated with a disruption or other mutations of the PTP36gene. The specification also fails to teach what specific condition is associated with the overall phenotype of uterine abnormality comprising keratin in the uterine horn or lumen, increased organ weight. The art does not recognize any disorders that are associated with the overall phenotype of increased liver, spleen, thymus weight, uterine dilation and presence of keratin in the uterine horns and lumen. As such, the claimed mouse is not a valid model for any disorder. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not credible, specific and substantial.

3) To identify agents having an effect on PTP36 expression or function. This asserted utility is not credible or substantial because the specification does not disclose 1) how to use a mouse or cell that does not express PTP36 to identify agents which affect the gene expression or function; 2) how to use a heterozygous PTP36 knockout mouse to identity agents which affect

the gene expression or function; 3) how to use such identified agents that affect PTP36 expression or function. This asserted utility is not credible since there is no expression or function can be monitored in the knockout mouse or cells/tissues isolated from said mouse, it is unclear how these agents that affect PTP36 expression/function can be identified. Claims 28, 37, 53, 55-57 encompass heterozygous knockout mouse. The heterozygous knockout mice usually have no difference in expression relative to a wild type mice. As such, a skilled artisan would not know how to use a heterozygous PTP36 knockout mouse to identify agents that have an affect on PTP36 expression. Further, the specification does not teach any use for the agents that have an effect on PTP36 expression or function. Since the identified agents do not have a substantial utility, the claimed mouse or mouse cells used in a method for identifying such agents does not have substantial utility as well.

4) To test and develop new treatments relating to the behavioral phenotypes. This utility is not credible, substantial and specific because the specification does not teach that the claimed mouse displays any behavioral abnormality. As such, it is not a valid model for any behavioral disorder. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not credible, specific or substantial.

Since the claimed transgenic mouse and cells/tissues isolated from said mouse does not have utility, the method for producing said transgenic mouse does not have utility either. Therefore, the claimed invention lacks patentable utility for reasons given above.

Claims 28-32, 37, 47, 52-54 and 57 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible,

substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, even if the claimed mouse has utility, it would require undue experimentation to make and use the invention as claimed.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the Invention:

Claims 28-32, 37, 47, 53-57 are drawn a transgenic mouse whose genome comprises a null allele in the endogenous PTP36 gene, wherein the null allele comprises a neo-lacZ selection marker, wherein the disruption is homozygous, the mouse exhibits phenotype of increased liver, spleen, thymus weight, wherein the female mouse exhibits uterine dilation, presence of keratin in uterine horns and lumen. The claims are further drawn to a cell or a tissue isolated from said transgenic mouse, and a method of producing said transgenic mouse.

Breadth of claims and amount of guidance in the specification and working Examples:

In the instant case, claims 28-32, 37, 47, 53-57 encompasses a transgenic mouse that comprises a null allele in the endogenous PTP36 gene. The specification does not provide an

enabling disclosure for how to use the transgenic mouse as claimed. The specification discloses a PTP36 transgenic knockout mouse, wherein the disruption is homozygous, the mouse exhibits phenotype of increased liver, spleen, thymus weight, wherein the female mouse exhibits uterine dilation, presence of keratin in uterine horns and lumen. The specification does not provide specific teaching on how to use these mice with the disclosed phenotype. The specification prophetically teaches that the transgenic mouse can be used to screen drugs or as models for diseases, or screening agents that modulates a phenotype of said mouse. However, the specification fails to teach what type of diseases are the disclosed phenotypes related to. The specification also fails to teach how to use the agent that modulates the phenotype associated with PTP36 gene disruption. As such, one skilled in the art would not know how to use the transgenic mouse with the phenotype of increased liver weight, for example, as a disease model or screen drugs for a specific disease. Moreover, the specification fails to teach how to use a cell or tissue isolated from the transgenic mouse. Therefore, the teaching of the specification is limited.

The state of art and the predictability in the art

The state of art at the time of the filing is silent on a transgenic mouse whose genome comprises a null allele in the endogenous PTP36 gene, wherein the disruption is homozygous, the mouse exhibits phenotype of increased liver, spleen, thymus weight, wherein the female mouse exhibits uterine dilation, presence of keratin in uterine horns and lumen, as compared to a wild type mouse. At the time of filing, the function of the PTP36 gene is unclear. *In vitro* experiments demonstrate that (Ogata et al.) over-expression of the murine PTP36 in Hela cells renders the cells to spread less well, grow more slowly and adhere to the extracellular matrix

protein less well, which suggests that PTP36 is involved in the regulation of cell adhesion, cell growth and cytoskeleton process. However, the art does not provide any teaching regarding the relationship between PTP36 function and the disclosed phenotype. The overall phenotype observed in the claimed mouse does not correlate to the hypothesized function of PTP36 which is involved in cell adhesion and cell growth. As such, whether the claimed mouse can be used as a model to study PTP36 in the process of cell adhesion and cell growth is unpredictable.

At the time of filing, the phenotype of the transgenic knockout mouse is considered unpredictable. One has to remember that many of the phenotypes examined in transgenic and knockout models are influenced by the genetic background in which they are studied and the effect of allelic variation and the interaction between the allelic variants (pg.1425, paragraph 1 in Sigmund, C.D. 2000. Arterioscler Thromb Vasc Biol.20:1425-1429). Further, the transgene expression and the physiological consequences of transgene products are not always accurately predicted in transgenic mouse studies (pg.62, paragraph1, lines 7-9 in Wall, R.J. 1996. Theriogenology 45:57-68). The particular genetic elements required for expression varies from species to species. Our lack of understanding of essential genetic control elements makes it difficult to design transgenes with predictable behavior (Wall, 1996). For example, Jacks et al. (1992) describe Rb knockout mice that do not display retinoblastoma; rather they exhibit the unexpected phenotype of pituitary tumors. The pituitary tumors arise from cells lacking a wild-type Rb allele. Thus, tumors were found to arise not in retinas, as in humans, but in the pituitary gland (page 299, Discussion, paragraphs 1 and 3). In the instant case, the function of the PTP36 *in vitro* is not predictive of its function *in vivo*. Thus, one skilled in the art would not know how

to use the claimed mouse with no phenotype (such as a heterozygote), or the phenotype which is independent of the transgene function.

The specification teaches that the claimed mouse can be used as disease models and used for screening drugs. However, a search of the prior art does not reveal any known disease which is correlated with the disclosed phenotypes. The mere statement from the specification that the mouse can be used as a disease model is so vague which renders it meaningless as a specific teaching for how to use said mouse. Without any guidance from the specification, one skilled in the art would engage in undue experimentation to determine how to use the claimed mouse for the disclosed embodiments. Therefore, the instant specification fails to enable the PTP36 knockout mouse as claimed.

(10) Response to Argument

Appellant's argument that using the PTP36 knockout mouse to study the function of the PTP36 gene is a well-established utility is not persuasive. Appellant is reminded that in MPEP, the guideline for the utility requirement clearly states: "An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible." Using the mice claimed "to study PTP36 gene function" is basic research. In other words, such studies would require analysis of the properties of the mice (phenotype analysis) or analysis of the processes in which they are involved (for example, analysis of increased organ weight, in which the mice are involved). Analysis of the phenotype is clearly basic research because it is studying the properties of the claimed product. Studying the role of the PTP36 gene within the realm of

uterine abnormality and increased organ weight is also basic research because it is studying the processes in which the mice and the PTP36 gene disruption are involved. Therefore, determining the phenotype of the mice and the studying processes in which the mice are involved are equivalent to the basic research examples described in the utility guidelines as not having "substantial utility." The MPEP states "the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities": A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved..." Accordingly, using the mice "to study PTP36 gene function" is not a "substantial utility" and, therefore, fails to be a "well-established" utility. Furthermore, while Appellants have taught how to analyze the phenotype of the knockout mice, Appellants have not taught how to study the function of the PTP36 gene within the realm of uterine abnormality and increased organ weight. Nor can any such studies be envisioned from the art at the time of filing. Without such guidance, Appellants have not provided the guideposts for one of skill to use the mice claimed to study the function of the PTP36 gene within the realm of uterine abnormality and increased organ weight. The utility guidelines specifically state that further research is not a "substantial utility." In the instant case, further study of mice would have been required to determine how to use the mouse of Appellant's invention to elucidate the function of PTP36 in the process of increased organ weight and uterine abnormality, further research would also be required to use the mice according to the embodiments described in the specification, for example, screening drugs for a disorder (because the phenotype does not reflect any disease in

human, and the specification fails to teach what disease the mouse model represents). Therefore, using the mice to study the function of the PTP36 gene is not a well-established utility.

In Re Fisher states: "Regarding the seven uses asserted by Fisher, we observe that each claimed EST uniquely corresponds to the single gene from which it was transcribed (underlying gene). As of the filing date of the '643 application, Fisher admits that the underlying genes have no known functions. Fisher, nevertheless, claims that this fact is irrelevant because the seven asserted uses are not related to the functions of the underlying genes. We are not convinced by this contention. Essentially, the claimed ESTs act as no more than research intermediates that may help scientists to isolate the particular underlying protein-encoding genes and conduct further experimentation on those genes. The overall goal of such experimentation is presumably to understand the maize genome – the functions of the underlying genes, the identity of the encoded proteins, the role those proteins play during anthesis, whether polymorphisms exist, the identity of promoters that trigger protein expression, whether protein expression may be controlled, etc. Accordingly, the claimed ESTs are, in words of the Supreme Court, mere "object[s] of use-testing," to wit, objects upon which scientific research could be performed with no assurance that anything useful will be discovered in the end. Brenner, 383 U.S. at 535." The instant case is similar to Fisher case that the function of PTP36, in context with the claimed phenotype, is unknown. Thus, the claimed mouse acts as no more than research intermediates that may help scientists to understand the function of PTP36, and what role it plays in observed phenotype of the claimed mouse. Therefore, such utility is not substantial.

Appellants point to an NIH report from 2004 and Austin (Nature Genetics, 2004, Vol. 36, No. 9, pg 921-924) to support that the claimed mouse has patentable utility. In response to

Appellant's argument, the examiner would point out that first, the NIH report and Austin were not available until 2004 and cannot be used to establish what was "well-established" at the time of filing. Second, while the NIH report suggests knockout mice may be models of disease, the specification does not identify that mice with uterine dilation, the appearance of keratin in the uterine horn and lumen, or increased organ weight as claimed as models of any disease, and they are not symptoms of any disease found in humans. Lastly, the references merely suggest using knockout mice to study the function of targeted genes, which does not rise to the level of a substantial utility according to the utility guidelines. The NIH report states knockout mice can be used to elucidate gene function. Austin states null-reporter alleles should be created as a starting point for studying the function of every gene. Appellant has used the mice in expression analysis and phenotype analysis tests, but Appellants have not determined the function of the gene. Simply using the mice for further research of the PTP36 gene is not a substantial utility for reasons set forth above. Moreover, the cited references do not teach a specific use for the claimed mouse. Appellant is again reminded that the examiner does not question the general utility of any knockout mouse, but only the utility of the claimed mouse, the PTP36 knockout mouse,. Neither of the references teaches a specific or substantial utility for mice with a disruption in the PTP36 gene as claimed.

Appellants also point to Albert (4th edition, Garland Science 2002), Lewin (Gene VII, Oxford press 2000), Joyner (Gene targeting: A practical approach, preface, Oxford University Press 2000), Matise (Production of Targeted Embryonic Stem Cell Clones, Oxford press 2000), Crawley (What's wrong with my mouse, Wiley-Liss 2000) and Doetschman (Laboratory Animal Science, 1999) to support that the claimed mouse have patentable utility. However, similar to

NIH report and Austin, these references merely teaches knockout mice can be used to study the function of targeted genes, which does not rise to the level of a substantial utility for reasons discussed above. In fact, the passage cited by Appellant from Albert states, "the ultimate goal in each case is to produce a collection of mutant strains in which every gene in the organism has either been systematically deleted, or altered such that it can be conditionally disrupted. Collection of this type will provide invaluable tool for investigating gene function on a genomic scale." It suggests that it is the collective information, rather than a single knockout mouse such as PTP36, that would provide an invaluable tool for investigating gene function on a genomic scale. Further, the statement cited by Appellant from Doetschman "the conclusion will be that the knockout phenotypes do, in fact, provide accurate information concerning gene function, that we should let the unexpected phenotypes lead us to the specific cell, tissue, organ culture, and whole animal experiments that are relevant to the function of the gene in question..." in fact suggests that further research is required to study the function of the gene. As such, it is not a substantial utility according to the utility guideline set forth in MPEP.

Appellant further assert that NIH has recently announced a three-year contract with Deltagen to procure knockout mice, thus the claimed mouse is useful. This argument is not persuasive because 1) it is unclear whether the claimed mouse PTP36 null mouse is among those that are purchased by NIH; 2) it is unclear how the mice and data are going to be used. If they are only used for basic research, it does not rise to the level of substantial utility for reasons given above. Merely selling a product does not contribute utility to that product.

Appellant's assertion that using the PTP36 knockout mice to study PTP36 function is a specific utility is not persuasive. For the references discussed above, none of them supports a

specific utility for the claimed mouse, a transgenic mouse having a null PTP36 allele. The utility that applies to any knockout mouse is not specific to the claimed invention. The case law states (*In Re Fisher*) that "Fisher's seven asserted uses are plainly not "specific." Any EST transcribed from any gene in the maize genome has the potential to perform any one of the alleged uses. That is, any EST transcribed from any gene in the maize genome may be a molecular marker or a source for primers. Likewise, any EST transcribed from any gene in the maize genome may be used to measure the level of mRNA in a tissue sample, identify the presence or absence of a polymorphism, isolate promoters, control protein expression, or locate genetic molecules of other plants and organisms. Nothing about Fisher's seven alleged uses set the five claimed ESTs apart from the more than 32,000 ESTs disclosed in the '643 application or indeed from any EST derived from any organism. Accordingly, we conclude that Fisher has only disclosed general uses for its claimed ESTs, not specific ones that satisfy §101." Similarly, the utility of the claimed mouse for studying the function of the disrupted gene is also a general use, one that can be applied to any knockout mouse. The argument of the mouse can only be used to study the function of PTP36 is not persuasive because the EST disclosed by Fisher can only be used as a probe for a specific sequence, however, the court decides that it does not set it apart from other ESTs. AS such, the using the claimed mouse to study gene function is not a specific utility.

Appellant point to Bradley et al. to demonstrate that each knockout mouse is specifically designed to disrupt a particular gene, thus use of each mouse is specific for studying the function of that disrupted gene. This argument is not persuasive for following reasons. The MPEP set forth that "A 'specific utility' is specific to the subject matter claimed. This contrasts with a

general utility that would be applicable to the broad class of the invention. Office personnel should distinguish between situations where an Appellant has disclosed a specific use for or application of the invention and situations where the Appellant merely indicates that the invention may prove useful without identifying with specificity why it is considered useful. For example, indicating that a compound may be useful in treating unspecified disorders, or that the compound has "useful biological" properties, would not be sufficient to define a specific utility for the compound...A general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Contrast the situation where an Appellant discloses a specific biological activity and reasonably correlates that activity to a disease condition. Assertions falling within the latter category are sufficient to identify a specific utility for the invention." In the instant case, the asserted utility of the claimed mouse for use as a disease model or screening drugs that for treating disorder is not a specific utility because the specification fails to teach what specific disease the claimed mouse represents and what type of drug can be screened using such model. The teaching of Bradley et al. merely indicate a specific locus within a gene can be targeted by a specific targeting construct. However, it does not provide a specific utility for the claimed mouse having a null PTP36 gene. The argument of the claimed mouse can only be used to study the function of PTP36 gene is not persuasive either. As discussed in the previous office actions, Olsen (GABA in the Nervous System, 2000, pg 81-95) taught that "although gene targeting is often useful in delineating the contribution of a given gene product to phenotypic characteristics observed, some gene knockouts lead to embryonic or perinatal lethality, and others lead to no apparent phenotype. This can arise from a lack of any role for the gene in question in regard to

the trait studies or from compensation by other gene products. Analysis of the compensation can yield valuable clues to the genetic pathway" (pg 82, last 11 lines of col. 1). Thus, knockout mice may not be capable of elucidating the function of the protein and may only provide a clue to a pathway the protein being knocked out is involved in. Using mice to obtain a clue to a pathway is not a "substantial utility." Using a mouse with a phenotype caused by genes compensating for a knocked out gene is not a "specific utility" because the phenotype is not specific to the knocked out gene. According to the example given in MPEP, the specification fails to establish a specific biological activity and reasonable correlates that activity to the null PTP36 allele.

Appellant's argument that actual use of the PTP36 knockout mouse to study gene function based on phenotype that is consistent with androgenization (lack of mammary tissue, uterine abnormality, increased anogenital distance) constitutes a real world use is not persuasive. The specification (page 49, lines 19-23) only teaches that female homozygous PTP36 knockout mouse displays the phenotype of lack of mammary tissue, presence of keratin in the uterine horn and lumen, and such phenotype suggests a hormonal imbalance, which is consistent of androgenization. However, the specification does not assert any use based on the observed phenotype. The term "androgenization" means a process of showing effects to androgen, which also means musculinization (defined by Mercksource.com). It further explains that it is a process of 1. the normal development of primary or secondary sex characters in the male. 2. the induction or development of male secondary sex characters in the female or prepubertal male, such as enlargement of the clitoris or penis, growth of facial and body hair, and deepening of the voice. 3. the condition of having such sex characters. The prior art teaches that clinical symptoms of hyperandrogenism in female include hirsutism, seborrhea, acne, hair loss,

clitoridean hypertrophism, voice alteration, mammary hypertrophism and muscular growth (see cited references, Exhibit Q and R). The overall phenotype of the claimed female mouse does not reflect such symptoms that are demonstrated in the human hyperadrogenism. Furthermore, if the PTP36 is involved in the androgenization process, it would also have produce androgenic effect in male mouse as well. The specification fails to teach what role PTP36 plays in the androgenization process except that female mice lack PTP36 expression lack mammary gland tissue, increased anogenital distance and producing keratin in uterine horn and lumen. In other words, the specification fails to establish the nexus between androgenization and the observed phenotype, hence the function of PTP36 in androgenization process. The prior art is silent on how to use the claimed mouse to study androgenization. Thus, the alleged use of the claimed mouse to study androgenization is not a well-established use because a person of ordinary skill in the art would not immediately appreciate why the invention is useful based on the characteristics of the invention. Furthermore, the specification fails to establish a substantial and specific use for the claimed mouse as a model to study androgenization. Therefore, since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not credible, specific or substantial.

Appellant argues that the data of the PTP36 knockout mouse has been incorporated into Deltabase, of which is subscribed by at least three largest pharmaceutical companies, and such commercial success demonstrate utility of the claimed mouse. Appellant is reminded that the subscription of a product does not automatically gives the product patentable use according to the statue of 35 U.S.C.101 and the utility guideline set forth in the MPEP. The subscription of the Deltabase by three largest company does not provide any information on how the

pharmaceutical companies would a) use the data; and/or which set of data to use. As discussed above, use of the collective information of the Deltabase does not give a patentable utility to a single product of which the information contains. As such, this argument is not persuasive.

Appellant argues that commercial sale of the PTP36 knockout mouse constitutes a real world use. This argument is found unpersuasive. The Declaration of Robert Driscoll (Exhibit K) asserts that the mouse is delivered to one large pharmaceutical company for studying gene function and for human therapeutic drug development. As discussed in above, using the claimed mouse to study the function of the PTP36 is only for a research use and an assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense. The pharmaceutical company may purchase the claimed mouse to conduct such research use, however, such use does not constitute a patentable utility for the claimed mouse. With regard to the use of the claimed mouse for human therapeutic drug development, it is not a specific use for the claimed mouse because the specification does not teach what specific disease the mouse model represents. Thus, it is unclear how this mouse can be used to develop human therapeutic drug, i.e. what type of disease the identified agent can treat. As discussed above, a general statement of development of human therapeutic drug, without specify which disease can be treated, is insufficient absent a disclosure of what condition can be treated (see MPEP regarding diagnosing disease cited above). Therefore, the alleged commercial success is not sufficient for providing a substantial and specific use for the claimed mouse.

Appellant argues that the claimed mouse is useful for validating the PTP36 gene as a "druggable" target. This argument is unpersuasive because the cited reference (Hopkins &

Groom) merely teaches that about 100 protein phosphatases are capable of serving as drug targets. However, it does not address whether PTP36 is a druggable target. As discussed above, an utility that applies to a genus of phosphatases is not specific to a specie (PTP36) per se. The teaching of Sands et al. again addresses the general use of knockout mouse which is highly predictive as to the on target effects and side effects of the associated drug, which is not specific to the claimed PTP36 knockout mouse. Elchebly et al. teach that PTP1B is validated as a target by the knockout mouse, and its inhibitors can be used to treat type 2 diabetes and obesity. Elchebly's teaching is based on prior knowledge that the PTP1B is implicated in insulin attenuation signal, and the phenotypic data obtained from the PTP1B knockout mouse confirms its role in insulin receptor activation and reflects that a PTP1B inhibitor's effects for potentially treating type 2 diabetes (see page 1544, abstract and 1st paragraph). However, in the instant case, the only function of PTP36 known in the prior art is its potential involvement in focal adhesion, there is no known function of the PTP36 in the context of androgenization of a female as alleged in Appellant's argument. Even the PTP36 knockout mouse may indicate the effect of a PTP36 inhibitor, one of ordinary skill in the art would not know the utility of said inhibitor because neither the prior art nor the specification teaches a use for such inhibitor, especially in the context of androgenization. Again, the teaching of Huijsduijnen addresses the use of knockout animals and antisenses or inhibitors for testing in disease models, it does not teach what type of model the claimed PTP36 knockout model represents. It does not teach what function of PTP36 has in the alleged androgenization of the female mouse. Even if the inhibitor of PTP36 can be developed and produces the same phenotype as in the PTP36 knockout mouse, it is unclear what

specific disease such inhibitor can treat. As such, the use of the PTP36 knockout mouse to validate the PTP36 gene as a "druggable" target is not a substantial and specific utility.

Appellant argues that the claimed mouse can be used as a model for studying the role of PTP36 in cancer cell metastasis. This argument is not persuasive because the specification does not disclose such utility. The references cited (both Wang et al. and Wadham et al.) are published after the filing date of the instant specification, which can only be used to confirm a disclosed utility. The 101 statue requires that one of ordinary skilled in the art would immediately appreciate why the invention is useful based on the characteristics of the invention. In the instant case, the post filing art cannot be relied upon to establish a substantial and specific use for the claimed mouse because the specification does not teach such utility. The disclosed phenotype of the claimed mouse does not reflect any metastatic cancer model, specifically, the claimed mouse cannot be used as a cancer model because the mouse does not exhibit any phenotype that correlated with cancer. The specification fails to teach how to use such a mouse, without phenotype of any cancer, to be a model for studying cancer metastasis. Moreover, even the post filing art fails to establish that a PTP36 knockout mouse can be used as a model for cancer metastasis. Wang et al. identifies a number of mutations for the PTP gene family, including PTP36, in colorectal cancer samples. However, the author also states that little is known about the function of the PTPs, including PTP36 (see page 1166, middle column, 2nd paragraph). Wadham identifies a substrate of PTP36, β catenin, indicating this protein is involved in adherens junction. The data disclosed in both reference at most pointing to a possible involvement of PTP36 with focal adhesion, and a possible involvement of PTP36 with colorectal cancer (it unclear whether it is causal or result from cancinogenesis process). None of

the references teaches a nexus between the PTP36 function and cancer metastasis. Without teaching from the specification, one of ordinary skilled in the art would not know how to use the claimed mouse, without any phenotype correlates with cancer metastasis, as a model for cancer metastasis based on the information disclosed by Wang et al. and Wadham et al. Therefore, using PTP36 knockout mouse to study cancer metastasis is not a credible, substantial and specific utility.

Appellant argues that the claimed mouse can be used to study expression of PTP36. This is not persuasive. Similar to the rationale of studying PTP36 function is not a substantial and specific utility, using the mouse comprising null-reporter to study gene expression is not a patentable utility studying the expression of a gene in which the function is unknown is not a substantial utility, whereas studying the expression of a gene using null-reporter is not a specific utility to the mouse comprising a null PTP36 allele. According to *In re fisher* as discussed above, studying PTP36 expression using the PTP36 knockout mouse does not set it apart from such use of other gene knockout mouse. The teaching of Austin merely indicates that inserting a reporter gene to any null allele allows a rapid assessment of which cell types normally support the expression of that gene, which is not a specific utility of the PTP36 knockout mouse.

For reasons set forth above, Appellant fails to establish a well-established use for the claimed mouse. The asserted utility in the instant specification is not substantial and specific either. Therefore, the claimed mouse, hence the method of making said mouse and cells isolated from said mouse, lack patentable utility.

Appellant assert that the position that the claimed mouse is enabled set forth in the office action mailed on 6/3/2003 is correct. Appellant is reminded that this rejection is corrected by the

subsequent full enablement rejection mailed on 4/23/04 for reasons set forth of the record and discussed in the subsequent office actions mailed on 12/16/04 and 3/22/05. The examiner reiterate the position that the claimed mouse lack utility for reasons discussed above, and lack enablement because the specification fails to teach how to use the claimed mouse according to the embodiments disclosed.

Appellant has not separately addressed the enablement rejection. As such, the 112 1st rejection stands for reasons set forth of the record and reiterated above.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Celine Qian, 1/30/06

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